

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 September 2004 (02.09.2004)

PCT

(10) International Publication Number
WO 2004/074491 A3

(51) International Patent Classification⁷: C12N 15/82,
C07K 14/415

(21) International Application Number:
PCT/EP2004/001427

(22) International Filing Date: 16 February 2004 (16.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/448,429 18 February 2003 (18.02.2003) US

(71) Applicant (for all designated States except US): SYN-
GETA PARTICIPATIONS AG [CH/CH]; Schwarzwald-
allee 215, CH-4058 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BROWN, Devon** [US/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB). **CAMPOS, Manuel** [CA/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB). **DALMIA, Bipin** [US/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB). **DEMAREST, Stephen** [US/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB). **HANSEN, Genevieve** [FR/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB). **HEIFETZ, Peter, Bernard** [US/GB]; Syngenta Limited, Jealott's Hill International Research Centre, Bracknell, Berks RG42 6YA (GB).

(74) Agents: **GAAL, Jozsef, Christopher et al.**; Intellectual Property Department, Syngenta Limited, Jealott's Hill International Research Centre, P.O. Box 3538, Bracknell, Berks RG42 6YA (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
18 November 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: EXPRESSION IN PLANTS OF ANTIBODIES AGAINST ENTEROTOXIGENIC *ESCHERICHIA COLI*

(57) Abstract: The present invention relates to the expression of antibodies and/or fragments thereof in plants, and in particular to the expression of antibodies and/or fragments thereof that have specificity for enterotoxigenic *Escherichia coli*. Nucleotide and amino acid sequences of such antibodies and/or fragments are disclosed, as are methods of producing such antibodies and/or fragments, transgenic plants expressing such antibodies and/or fragments thereof, and methods of using such transgenic plants or material derived therefrom, in particular in the treatment or prevention of enteric disease. Also described are methods of enhancing the stability of antibodies and fragments thereof.

WO 2004/074491 A3

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/EP2004/001427

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/82 C07K14/415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, EMBL, BIOSIS, EMBASE, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	DEMAREST S J ET AL: "Optimization of the Antibody CH3 Domain by Residue Frequency Analysis of IgG Sequences" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 335, no. 1, 2 January 2004 (2004-01-02), pages 41-48, XP004476444 ISSN: 0022-2836 the whole document	1-8
P, A	TEKOA H Y ET AL: "Controlled glycosylation of therapeutic antibodies in plants" ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, NEW YORK, US, US, vol. 426, no. 2, 15 June 2004 (2004-06-15), pages 266-278, XP004509803 ISSN: 0003-9861	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *A* document member of the same patent family

Date of the actual completion of the international search

9 August 2004

Date of mailing of the international search report

30.09.04

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Keller, Y

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/001427

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>THIES M J W ET AL: "Folding and Oxidation of the Antibody Domain CH3" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 319, no. 5, 21 June 2002 (2002-06-21), pages 1267-1277, XP004449701 ISSN: 0022-2836</p>	
A	<p>KACSKOVICS I ET AL: "The heterogeneity of bovine IgG2: VIII. The complete cDNA sequence of bovine IgG2a (A2) and an IgG1" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 33, no. 2, 1996, pages 189-195, XP002273988 ISSN: 0161-5890</p>	
A	<p>SYMONS D B A ET AL: "STRUCTURE OF BOVINE IMMUNOGLOBULIN CONSTANT REGION HEAVY CHAIN GAMMA 1 AND GAMMA 2 GENES" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 26, no. 9, 1989, pages 841-850, XP009027972 ISSN: 0161-5890</p>	
A	<p>WO 00/20612 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH); GRIOT WENK MONIKA ELS) 13 April 2000 (2000-04-13)</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/001427

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-8, 41-57 and 35-40, 58 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8, 41-57 and 35-40, 58 partially

Stabilised IgG through Ch2, Ch3, optimisation.

2. claims: 11, 12, 13-40, 58-60 (partially)

VH domain specific for K99 antigen (SEQ ID No 2) and related subject matter

3. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K99 antigen (SEQ ID No 1) and related subject matter

4. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VL domain specific for K99 antigen (SEQ ID No 3) and related subject matter.

5. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88 antigen (SEQ ID No 5) and related subject matter

6. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88 antigen (SEQ ID No 7) and related subject matter

7. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88 antigen (SEQ ID No 9) and related subject matter

8. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88 antigen (SEQ ID No 11) and related subject matter

9. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88antigen (SEQ ID No 13) and related subject matter

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 9, 10, 13-40, 58, 59, 60 (partially)

VH domain specific for K88 antigen (SEQ ID No 15) and
related subject matter

11. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K99 antigen (SEQ ID No 4) and related
subject matter

12. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K88 antigen (SEQ ID No 6) and related
subject matter

13. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K88 antigen (SEQ ID No 8) and related
subject matter

14. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K88 antigen (SEQ ID No 10) and
related subject matter

15. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K88 antigen (SEQ ID No 12) and
related subject matter

16. claims: 11, 12, 13-40, 58-60 (partially)

VL domain specific for K88 antigen (SEQ ID No 14) and
related subject matter

17. claims: 11, 12, 13-40, 58-60 (partially)

VH domain specific for K88 antigen (SEQ ID No 16) and
related subject matter

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/001427

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0020612	A	13-04-2000	AU 758817 B2	03-04-2003
			AU 6334099 A	26-04-2000
			BR 9915919 A	21-08-2001
			CA 2344269 A1	13-04-2000
			CN 1330718 T	09-01-2002
			WO 0020612 A2	13-04-2000
			EP 1117817 A2	25-07-2001
			HU 0103616 A2	28-01-2002
			JP 2002526116 T	20-08-2002
			PL 347904 A1	22-04-2002
			TR 200101032 T2	22-10-2001
			ZA 200102814 A	05-06-2002